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PAPER

Unsymmetric salen ligands bearing a Lewis base: intramolecularly cooperative catalysis for cyanosilylation of aldehydes†

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A series of unsymmetric salen ligands derived from 1,2-diaminocyclohexane bearing an appended Lewis base on the three-position of one aromatic ring were synthesized by the reaction of various functional salicyaldehydes with the condensation product of 1,2-diaminocyclohexane mono(hydrogen chloride) and 3,5-di-*tert*-butylsalicylaldehyde. These ligands in conjunction with Ti(O^iPr)$_4$ exhibited excellent activity in catalyzing the cyanosilylation of aldehydes with trimethylsilyl cyanide (TMSCN) at mild conditions. The highest activity was observed in the catalyst system with regard to the salen ligand bearing a diethylamino group, which proved to be active even at a high [aldehyde]/[catalyst] ratio up to 50000. In a low catalyst loading of 0.05 mol%, the quantitative conversion of benzaldehyde to the corresponding cyanosilylation product was found within 10 min. at ambient temperature. An intramolecularly cooperative catalysis was proposed wherein the central metal Ti(IV) is suggested to play a role of Lewis acid to activate aldehydes while the appended Lewis base to activate TMSCN.

Introduction

Cyanation reaction of carbonyl compounds is one of the important methods for forming new C–C bonds. The resulting cyanohydrins are versatile synthetic intermediates in organic chemistry. Owing to the hydroxyl and nitrile groups, they can be transformed into a variety of valuable functional compounds, such as α-hydroxy acids, α-hydroxy aldehydes, β-hydroxy amines, and α-amino acid derivatives.[1] The cyanosilylation of aldehydes with trimethylsilyl cyanide (TMSCN) is the much-studied reaction for synthesizing cyanohydrins. Numerous catalyst systems, including Lewis acids,[2] Lewis bases,[3] *N*-heterocyclic carbenes,[4] metal complexes,[5] inorganic salts,[1e,6] and bifunctional catalysts,[7] have been developed for this transformation. Among them, Lewis acid–base bifunctional catalyst systems are more efficient for this reaction. The first example reported by Shibasaki *et al.*[8] in 1999 is a BINOL-based bifunctional catalyst. In this system, dual activation mechanism where the two substrates were activated simultaneously at defined position was proposed. Although the products were obtained generally with excellent enantiomeric excess, high catalyst loading up to 9 mol% and the addition of phosphine oxide up to 36 mol% are prerequisite for efficient transformation. Following this work, Nájera *et al.*[9] designed a monometallic bifunctional catalyst BINOLAM-AlCl for this reaction. Notably, the ligand could be recovered by a simple method, and reused without loss of activity. Slight modification of this catalyst by replacing diethyl amine group with morpholine, the resulting complex proved to be more effective catalyst for the cyanosilylation involving aliphatic aldehyde.[10] Kim[11] and Trost[12] independently developed Proline-derived catalysts for this reaction. Feng and coworkers synthesized *N*,*N*′-dioxide-Ti(O^iPr)$_4$ bifunctional catalyst for the asymmetric cyanosilylation of aldehydes.[13] Tang *et al.*[14] chose cyclic *o*-hydroxylarylphosphonodiamides as ligands for asymmetric trimethylsilylcyanation of aromatic aldehydes. You and coworkers[15] reported non-C_2-symmetric BINOL-based bifunctional catalyst, which showed active in the absence of any additive. Salen-Ti complexes have been proved to be effective catalysts in the asymmetric cyanosilylation of aldehydes.[5a,16] In the continuation of our work on intramolecularly cooperative catalysis,[17] we have designed a series of unsymmetric salen ligands (Fig. 1) bearing an appended Lewis base on the three-position of one aromatic ring and applied them to the cyanosilylation of aldehydes and TMSCN by the combination with Ti(O^iPr)$_4$, in which the central metal ion is expected to play a role of Lewis acid to activate aldehydes while the appended Lewis base to activate TMSCN.

Results and discussion

The unsymmetric salen ligands **L1**, **L2** and **L4–L9** derived from 1,2-diaminocyclohexane in Fig. 1 were synthesized by the reaction of the corresponding functional salicyaldehydes with the condensation product of 1,2-diaminocyclohexane mono(hydrogen chloride) and 3,5-di-*tert*-butylsalicylaldehyde.[18] And symmetrical ligand **L3** was obtained through the condensation of aldehyde and 1,2-diaminocyclohexane. The key is the preparation of various functional salicyaldehydes. All ligands were obtained in moderate yields and characterised by NMR and HRMS.†

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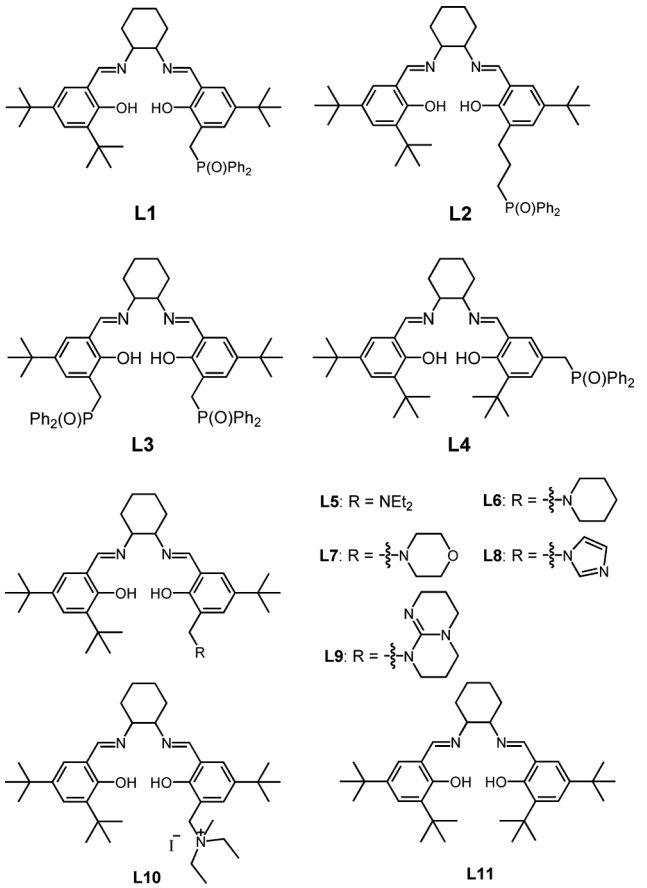
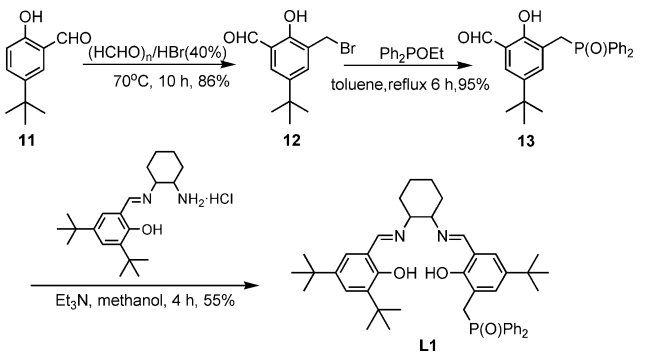


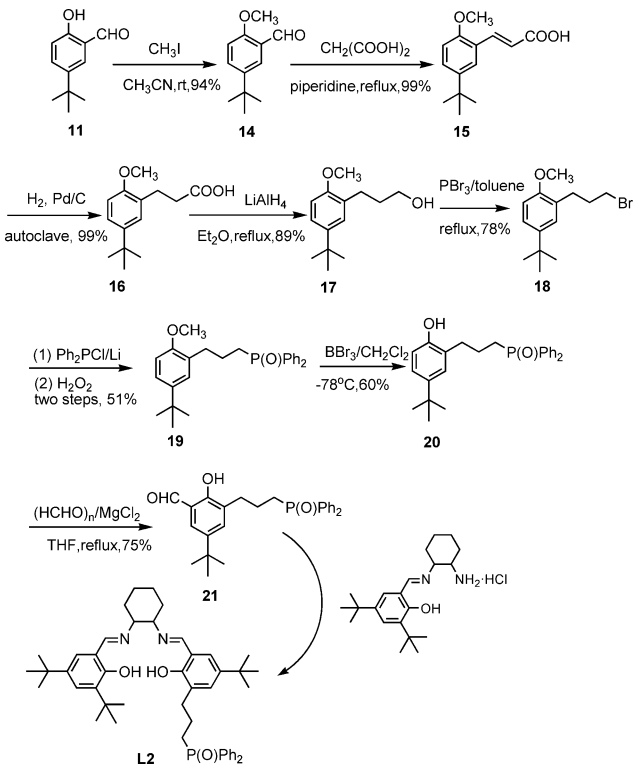
Fig. 1 Various salen ligands.

Ligand **L1** bearing a phosphane oxide on the three-position of one aromatic ring was synthesized with 5-*tert*-butyl-2-hydroxybenzaldehyde **11** as starting material according to the following procedure (Scheme 1). 3-(bromomethyl)-5-*tert*-butyl-2-hydroxybenzaldehyde **12** was first prepared by the bromomethylation of compound **11**. Then Arbusov reaction was carried out between compound **12** and $Ph_2POC_2H_5$, affording the corresponding phosphane oxide **13**.[19] Finally, the reaction of compound **13** and the condensation product of 1,2-diaminocyclohexane mono(hydrogen chloride) with 3,5-di-*tert*-butylsalicylaldehyde provided the unsymmetrical salen ligand **L1**.



Scheme 1 Synthesis of ligand **L1**.

In order to examine the influence of the linker between salen ligand framework and phosphane oxide on the catalytic activity, ligand **L2** containing a long spacer was synthesized using 5-*tert*-butyl-2-hydroxybenzaldehyde **11** as starting material. In the procedure of synthesizing this ligand, the preparation of 5-*tert*-butyl-3-(3-(diphenyl-phosphoryl)propyl)-2-hydroxybenzaldehyde **20** is a key step. It can be synthesized *via* an eight-step sequence from compound **11**. The bromo-compound **18** was converted to the phosphine oxide **19** *via* a coupling reaction with the lithiation product of diphenylphosphinic chloride, followed by oxidation with H_2O_2. Through deprotection and formylation in turn, we finally achieved compound **21**. Ligand **L2** came to hand after two-step sequential condensations (Scheme 2).[17a,20]

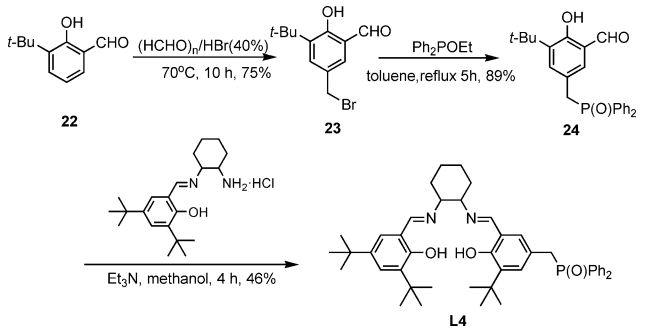


Scheme 2 Synthesis of ligand **L2**.

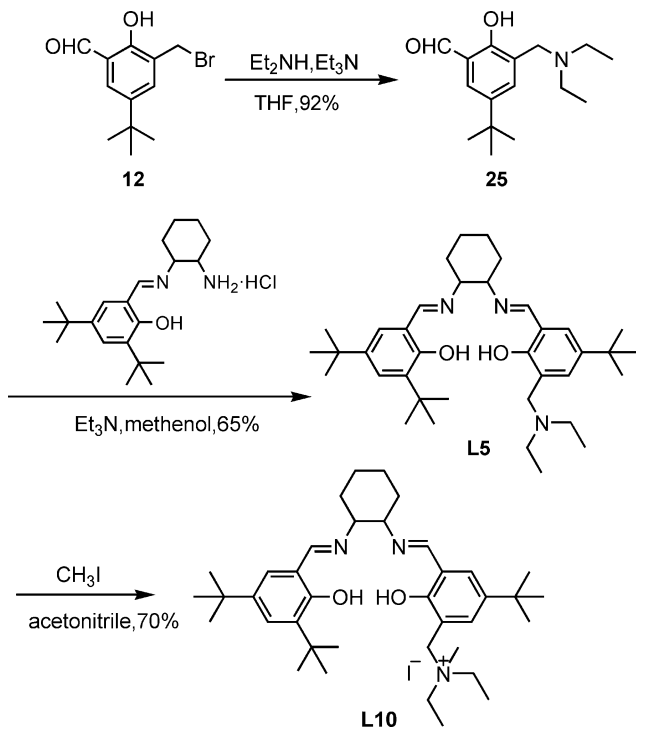
For a comparison purpose, symmetrical ligand **L3** that possessed two phosphane oxide groups on both 3- and 3′-position was synthesized by reaction of **13** and 1,2-diaminocyclohexene. Ligand **L4** in which the phosphane oxide group was appended on the 5-position of one aromatic ring was also synthesized through a similar procedure of **L1** starting with 3-*tert*-butyl-4-hydroxybenzaldehyde (Scheme 3).

To investigate the influence of basicity of the functional group appended on the salen ligand framework, ligand **L5** in which diethylamino group instead of diphenylphosphane oxide is attached on the ligand framework was synthesized. As shown in Scheme 4, direct addition of diethylamine to 3-(bromomethyl)-5-*tert*-butyl-2-hydroxybenzaldehyde **12** afforded compound **25**,[21] then ligand **L5** came to hand through the reaction with condensation product of 1,2-diaminocyclohexane mono(hydrogen chloride) and 3,5-di-*tert*-butylsalicyladehyde.

Additionally, a series of functionalized salen ligands **L6–L9** were synthesized in a similar procedure of **L1** for further studying the effect of stereo-hindrance of the appended Lewis base (Scheme 5). Furthermore, ligand **L10** bearing a quaternary ammonium salt



Scheme 3 Synthesis of ligand **L4**.

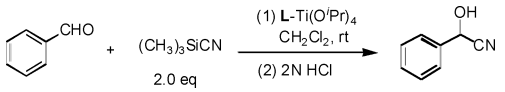


Scheme 4 Synthesis of ligands **L5** and **L10**.

on the three-position of one aromatic ring was also synthesized. It is relatively easy to prepare *via* simple quaterisation of ligand **L5** with CH_3I (Scheme 4).

We started our investigation with cyanosilylation of benzaldehyde at room temperature, with the use of ligand **L1**. Initially, the catalytic system was prepared by ligand **L1** combined with $Ti(O^iPr)_4$ in CH_2Cl_2 in a glove box at room temperature for 2 h, then benzaldehyde and TMSCN was added. We delightedly found that in the presence of 1 mol% of **L1**/$Ti(O^iPr)_4$ the reaction proceeded smoothly at room temperature to give an excellent yield up to 99% after 4 h (Table 1, entry 1). The similar result was obtained in the catalyst system regarding ligand **L2** (Table 1, entry 2), indicating that the linker length between salen framework and phosphane oxide has no obvious influence on the catalytic activity. For a comparison purpose, we also performed Jacobsen salen ligand **L11** together with $Ti(O^iPr)_4$ as catalyst (1 mol% loading) for this reaction, in the presence of 1 equimolar Ph_3PO. Only 70% yield was found in the resulting catalyst system with a prolonged reaction time of 24 h. This result indicates that the appended

Table 1 Addition of TMSCN to benzaldehyde using bifunctional catalysts[a]



Entry	Ligand	Substrate: Catalyst	Time	Yield (%)[b]
1	**L1**	100: 1	4 h	99
2	**L2**	100: 1	4 h	96
3	**L3**	100: 1	3 h	99
4	**L4**	100: 1	24 h	70
5	**L5**	100: 1	10 min.	99
6	**L6**	100: 1	1 h	97
7	**L7**	100: 1	3 h	< 5
8	**L8**	100: 1	3 h	98
9	**L9**	100: 1	40 min.	99
10	**L10**	100: 1	24 h	98
11	**L5**	200: 1	10 min.	99
12	**L5**	1000: 1	10 min.	97
13	**L5**	2000: 1	10 min.	97
14	**L5**	5000: 1	90 min.	99
15	**L5**	50000: 1	24 h	58

[a] All reactions were carried out in 2.5 mL CH_2Cl_2 at room temperature. [b] Isolated yield.

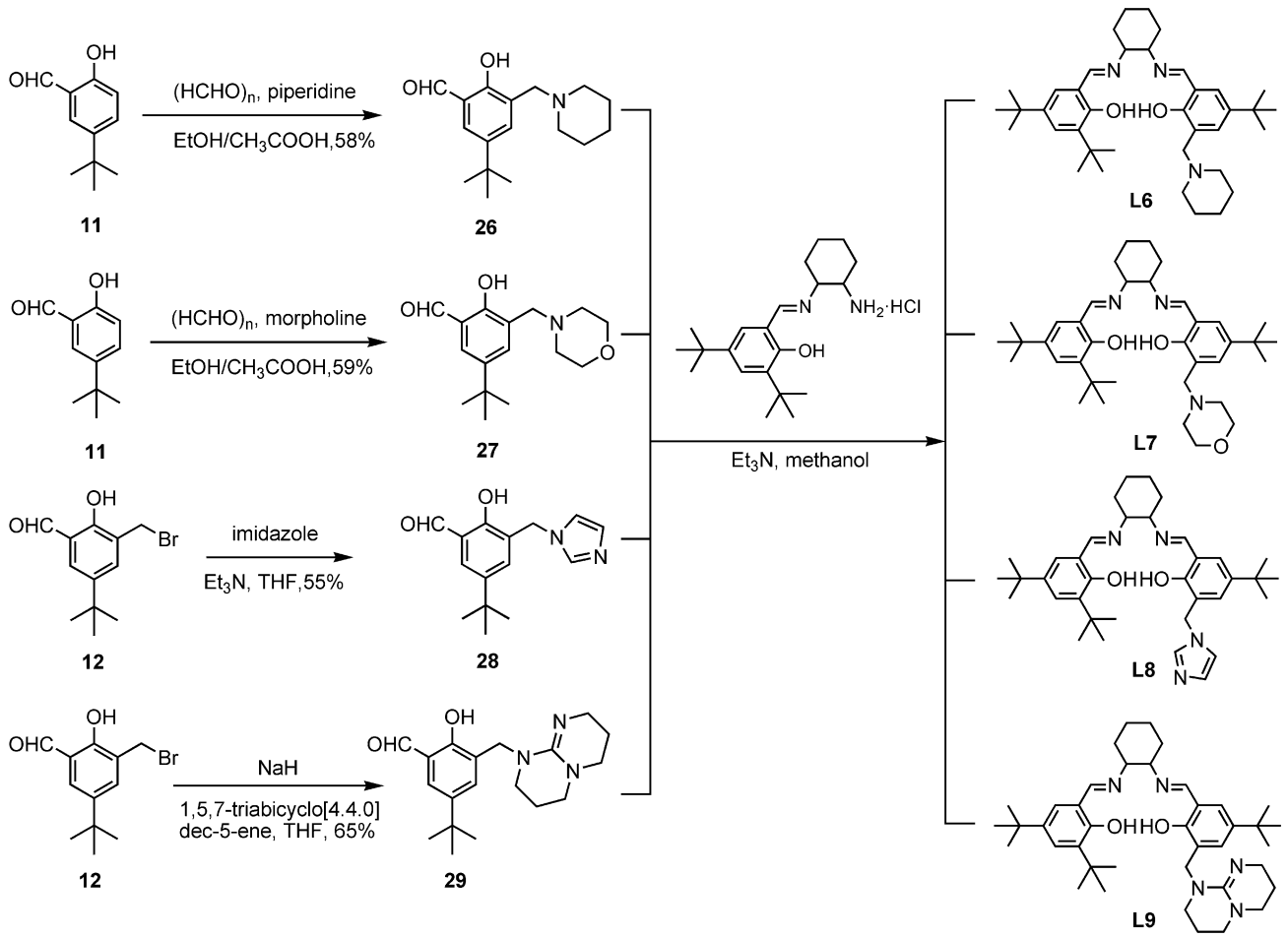
phosphane oxide on the salen ligand **1** or **2** is more beneficial to cooperatively catalyzing this reaction than free Ph_3PO.

As expected, the catalyst system with regard to the symmetrical ligand **L3** exhibited higher activity (Table 1, entry 3) than that concerning ligand **1** or **2** case. Interestingly, ligand **L4** with a diphenylphosphane oxide appended on 5-position of one aromatic ring in conjunction with $Ti(O^iPr)_4$ showed a very low activity (Table 1, entry 4), comparable to the catalyst system consisted of ligand **11**, Ph_3PO and $Ti(O^iPr)_4$. It is tentatively ascribed to the far distance between the Lewis acid and Lewis base in the system concerning **L4**, which is unfavourable to bring the activated TMSCN into appropriate position for attacking aldehyde coordinated to titanium.

Surprisingly, the catalyst system based on **L5–L9** exhibited more active for the cyanosilylation of TMSCN with benzaldehyde (Table 1, entries 5–9). The highest activity was observed in the catalyst system with regard to ligand **L5** bearing a diethylamino group (Table 1, entries 5, 11–15). In a low catalyst loading of 0.05 mol%, the quantitative conversion of benzaldehyde to the corresponding cyanosilylation product was found within 10 min. at ambient temperature, with a TOF (turnover frequency) up to 12000 h^{-1} (Table 1, entry 13). Notably, even at a high [aldehyde]/[catalyst] ratio up to 50000, the catalyst system consisted of ligand **L5** and $Ti(O^iPr)_4$ also exhibited excellent activity (Table 1, entry 15).

However, the catalyst system concerning ligand **L10** with an appended quaternary ammonium salt showed very low activity for this reaction under the same conditions. No or little product was found when the reaction was performed 1 h. Only with a prolonged time of 24 h and 1 mol% catalyst loading, quantitative conversion of benzaldehyde to 2-hydroxy-2-phenylacetonitrile was found (Table 1, entry 10). The results demonstrated the important role of the Lewis basicity of the appended functional group.

Although much effort was paid to isolate the metal complex from the mixtures of salen ligands and $Ti(O^iPr)_4$, we failed to obtain the single crystal for structure determination. It is obvious



Scheme 5 Synthesis of ligands **L6–L9**.

that both the central metal ion and the appended functional group on the ligand framework play important roles in synergistically catalyzing this reaction. We tentatively propose a synergistic mechanism wherein the central metal Ti(IV) is suggested to play a role of Lewis acid to activate aldehydes while the appended Lewis base to activate TMSCN.

For further confirming the intramolecular cooperation catalysis, some control experiments were performed. Plots of conversion *versus* reaction time are showed in Fig. 2. The rapid conversion of benzaldehyde was observed in the catalyst system regarding ligand **L5** rather than **L11**/Et_3N. For example, in the cyanosilylation of benzaldehyde with TMSCN at a condition of [benzaldehyde]/[catalyst] ratio of 10000 at room temperature, more than 70% conversion occurred at **L5**/Ti(O^iPr)$_4$ system within 80 min., while only 20% conversion was observed in the catalyst system of **L11**/Ti(O^iPr)$_4$ and Et_3N. This result indicates that an intramolecularly synergistic effect exists in the **L5**/Ti(O^iPr)$_4$ catalyst system for the cyanosilylation of aldehyde with TMSCN.

Moreover, we also explored the asymmetric cyanosilylation of benzaldehyde with TMSCN by the use the chiral ligands. Unfortunately, the enantioselectivity of the product was not satisfactory, an enantiomeric excess of 81% was observed in the catalyst system with respect to ligand **L5** at ambient temperature. The decrease of reaction temperature (even decreased to –40 °C) did not cause a distinct enhancement in enantioselectivity (see ESI, Table S1†).

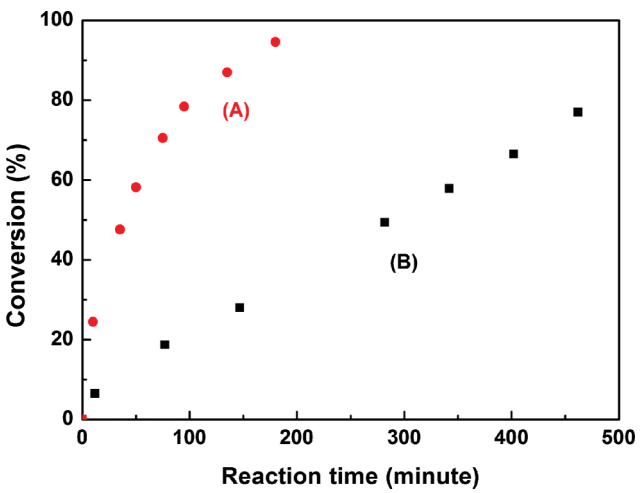
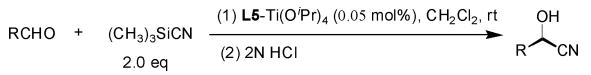


Fig. 2 Conversion of benzaldehyde with the use of (A) **L5**/Ti(O^iPr)$_4$, and (B) **L11**/Ti(O^iPr)$_4$ and Et_3N (1 equiv. to **L11**) as catalyst for the cyanosilylation with TMSCN at a condition of [benzaldehyde]/[catalyst] ratio of 10000 at room temperature.

Table 2 Synthesis of cyanohydrins using **L5** as ligand[a]



Entry	*R*	t (h)	Yield (%)[b]	*ee* (%)[c]
1	Ph	0.2	99	81
2	4-MeC_6H_4	2	99	80
3	4-$MeOC_6H_4$	4	26	88
4	2-$MeOC_6H_4$	4	57	50
5	4-$NO_2C_6H_4$	1	99	2
6	4-ClC_6H_4	1	99	68
7	PhCH=CH	0.5	99	–[d]
8		1	92	58
9	$CH_3(CH_2)_6$	0.5	97	–[d]
10	$(CH_3)_2CH$	0.5	99	–[d]

[a] All reactions were carried out in 2.5 mL CH_2Cl_2 at room temperature, with a ratio of aldehyde/catalyst of 2000 : 1. [b] Isolated yield. [c] The enantiomeric excess was determined by Agilent HPLC after the products were converted to the corresponding acetylesters. [d] Not measurable.

Furthermore, the catalytic system of ligand **L5** in conjunction with $Ti(O^iPr)_4$ was successfully applied to the cyanosilylation of other aromatic aldehydes with TMSCN (Table 2). In the presence of 0.05 mol% catalyst loading at ambient temperature, substituted benzaldehydes with an electron-donating group exhibited significantly low reactivity in comparison with benzaldehyde (Table 2, entry 2–4). On the contrary, 4-nitrobenzaldehyde and 4-chlorobenzaldehyde showed excellent reactivity in the cyanosilylation with TMSCN and was completely transformed into the corresponding products within 1 h (Table 2, entries 5 and 6).

Encouraged by the results of aromatic aldehydes with **L5**/$Ti(O^iPr)_4$, we also investigated some aliphatic aldehydes. To our delight, the catalytic system was compatible with aliphatic aldehydes, including α,β-unsaturated, functionalized, liner, and branched substrates (Table 2, entries 7–10). Excellent yields (92–99%) were obtained in the low catalyst loading of 0.05 mol% within 0.5 or 1 h.

Experimental

General information

^1H, ^{13}C and ^{31}P NMR spectra were recorded on a Varian INOVA-400 MHz type (^1H, 400 MHz; ^{13}C, 100 MHz; ^{31}P, 161 MHz) spectrometer. Their peak frequencies were referenced *versus* an internal standard (TMS) shifts at 0 ppm for ^1H NMR and against the solvent, chloroform-*d* at 77.0 ppm for ^{13}C NMR, phosphinic acid (85%) as an external standard for ^{31}P NMR respectively.

High resolution mass spectrometry (HRMS) was performed on a Micromass Q-Tof (Micromass, Wythenshawe, UK) mass spectrometer equipped with an orthogonal electrospray source (Z-spray).

Infrared spectra (IR) were measured using a Nicolet NEXUS FT-IR spectrophotometer equipped with a temperature-controlled high-pressure liquid cell (Harrick Scientific Corporation).

All manipulations involving air- and/or water-sensitive compounds were carried out in a glove box or under dry nitrogen using standard Schlenk techniques. All aldehydes, $Ti(O^iPr)_4$ and TMSCN, which were purchased from Acros company, were vacuum distillated before use. Dichloromethane (CH_2Cl_2) and acetonitrile were refluxed and distilled over CaH_2 under nitrogen atmosphere. Methanol was distilled from $Mg(OCH_3)_2$ under nitrogen. Tetrahydrofuran (THF) and toluene were distilled from sodium/benzophenone.

Synthesis of ligand L1–L10

General procedure for unsymmetric ligands (L1,L2,L4–L9). A dry flask charged with 1,2-diaminocyclohexane mono(hydrogen chloride) (2.0 mmol),[18] some 5 Å molecular sieve, and anhydrous methanol. 3,5-Di-*tert*-butyl-2-hydroxybenzaldehyde (2.4 mmol) was added in one portion and the reaction mixture was stirred at room temperature for 1 h. Then triethylamine (0.6 mL) was added, followed by the addition of the other aldehyde (1.6 mmol) dissolved in ethanol. After stirring at room temperature for another 4 h, some dichloromethane was added to dissolve the Schiff base, then the mixture was filtered to remove molecular sieve. Then the combined solvent was evaporated. The residue was purified by column chromatography on silica gel twice using petrol ether/ethyl acetate (10 : 1, 1% Et_3N) and dichloromethane/methanol (10 : 1) respectively as mobile phase to give the unsymmetric salen ligand as yellow solid.

L1. Yield: 55%. mp 84–86 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 13.67 (s, 1H), 13.49 (s, 1H), 8.28 (s, 1H), 8.23 (s, 1H), 7.66–7.77 (m, 4H), 7.30–7.45 (m, 6H), 7.25 (d, J = 2.8 Hz, 1H), 7.17 (s, 1H), 7.01 (d, J = 2.0 Hz, 1H), 6.95 (s, 1H), 3.62–3.86 (m, 2H), 3.23–3.33 (m, 2H), 1.43–1.88 (m, 8H), 1.40 (s, 9H), 1.23 (s, 9H), 1.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.66, 165.16, 158.09, 156.99 (d, J = 5.3 Hz), 140.67 (d, J = 3.1 Hz), 140.09, 136.55, 133.62, 133.26, 132.64, 132.28, 131.58 (d, J = 2.7 Hz), 131.50, 131.30 (d, J = 1.3 Hz), 131.21 (d, J = 1.4 Hz), 128.42, 128.36, 128.29, 128.23, 126.92, 126.82, 126.06, 118.71, 118.63, 117.93, 117.65, 72.55, 72.41, 35.08, 34.18, 33.82, 33.54, 33.19, 31.58, 31.28, 30.62, 29.93, 29.54, 24.39 (d, J = 4.5 Hz); ^{31}P NMR (161 MHz, $CDCl_3$): δ 31.92; IR (KBr): 3056, 2955, 2862, 1629, 1475, 1438, 1362, 1276, 1201, 1120, 733, 721, 695 cm^{-1}; HRMS (ESI): m/z Calcd. for $C_{45}H_{58}N_2O_3P$ $[M + H]^+$: 705.4185, found: 705.4186.

L2. Yield: 52%. mp 77–79 °C;^1H NMR (400 MHz, $CDCl_3$): δ 13.71 (s, 1H), 13.40 (s, 1H), 8.29 (s, 1H), 8.26 (s, 1H), 7.66–7.71 (m, 4H), 7.40–7.49 (m, 6H), 7.30 (d, J = 2.4 Hz, 1H), 7.08 (d, J = 2.0 Hz, 1H), 6.98 (d, J = 2.4 Hz, 1H), 6.96 (d, J = 2.0 Hz, 1H), 3.27–3.34 (m, 2H), 2.65–2.79 (m, 2H), 2.28–2.35 (m, 2H), 1.44–1.96 (m, 10H), 1.40 (s, 9H), 1.22 (s, 9H), 1.19 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.67, 165.31, 157.97, 156.82, 140.74, 139.90, 136.37, 135.21, 133.67 (d, J = 5.0 Hz), 132.72 (d, J = 5.1 Hz), 131.56, 130.88 (d, J = 2.1 Hz), 130.79 (d, J = 2.2 Hz), 129.92, 128.62, 128.51, 127.78, 126.77, 126.08, 126.02, 117.82, 117.57, 72.76, 72.20, 34.96, 34.06, 33.84, 33.44, 33.08, 31.42 (d, J = 6.9 Hz), 30.82, 30.66, 29.76, 29.43, 29.05, 24.28 (d, J = 7.1 Hz), 21.47 (d, J = 3.2 Hz); ^{31}P NMR (161 MHz, $CDCl_3$) δ 32.70; IR (KBr): 3056, 2956, 2862, 1628, 1473, 1438, 1362, 1272, 1175, 1120, 716, 695 cm^{-1}; HRMS (ESI): m/z Calcd. for $C_{47}H_{62}N_2O_3P$ $[M + H]^+$: 733.4498, found: 733.4511.

L4. Yield: 40%. mp 102–104 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 13.90 (s, 1H), 13.66 (s, 1H), 8.30 (s, 1H), 8.17 (s, 1H), 7.66–7.71

(m, 2H), 7.56–7.61 (m, 2H), 7.37–7.45 (m, 6H), 7.31 (d, J = 2.0 Hz, 1H), 6.98 (d, J = 2.4 Hz, 1H), 6.87 (s, 1H), 6.60 (s, 1H), 3.47–3.52 (m, 2H), 3.29–3.32 (m, 2H), 1.86–1.93 (m, 4H), 1.46–1.71 (m, 4H), 1.41 (s, 9H), 1.23 (s, 9H), 1.18 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.77, 165.22, 159.38 (d, J = 2.5 Hz), 158.00, 139.89, 136.84 (d, J = 2.3 Hz), 136.40, 132.92, 132.49, 131.95, 131.80 (d, J = 2.6 Hz), 131.71, 131.51, 131.42, 131.31 (d, J = 4.2 Hz), 131.20, 131.14, 131.09, 128.56, 128.44 (d, J = 2.2 Hz), 128.31, 126.79, 125.97, 119.44 (d, J = 8.0 Hz), 118.58 (J = 2.3 Hz), 117.82, 72.51, 72.05, 37.80, 37.13, 34.98, 34.51, 34.04, 33.24, 33.11, 31.44, 29.47, 29.12, 24.28; ^{31}P NMR (161 MHz, $CDCl_3$): δ 29.53. IR (KBr): 3057, 2953, 2862, 1629, 1468, 1439, 1389, 1361, 1272, 1201, 737, 718, 695 cm^{-1}; HRMS (ESI): m/z Calcd. for $C_{45}H_{58}N_2O_3P$ [M + H]$^+$: 705.4185, found: 705.4188.

L5. Yield: 65%. mp 110–111 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.72 (s, 1H), 8.32 (s, 1H), 8.27 (s, 1H), 7.41 (s, 1H), 7.30 (s, 1H), 7.05 (s, 1H), 6.98 (s, 1H), 3.57–3.67 (m, 2H), 3.25–3.36 (m, 2H), 2.57–2.55 (m, 4H), 1.45–1.95 (m, 8H), 1.41 (s, 9H), 1.24 (s, 18H), 1.06 (t, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.71, 164.92, 158.04, 157.12, 140.50, 139.85, 136.37, 130.25, 126.72, 126.11, 117.86, 117.75, 72.82, 72.35, 51.43, 47.06, 34.97, 34.07, 33.90, 33.40, 33.17, 31.47, 31.42, 29.45, 24.36, 24.32, 11.79; IR (KBr): 2962, 2864, 2798, 1630, 1468, 1441, 1361, 1266 cm^{-1}; HRMS (ESI): m/z Calcd. for $C_{37}H_{58}N_3O_2$ [M + H]$^+$: 576.4529, found: 576.4533.

L6. Yield: 69%. mp 83–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.71 (s, 1H), 8.31 (s, 1H), 8.27 (s, 1H), 7.38 (s, 1H), 7.31 (d, J = 2.4 Hz, 1H), 7.06 (s, 1H), 6.99 (d, J = 2.4 Hz, 1H), 3.51–3.59 (m, 2H), 3.27–3.34 (m, 2H), 2.44 (s, 4H), 1.43–1.92 (m, 14H), 1.41 (s, 9H), 1.23 (s, 18H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 165.69, 165.07, 158.00, 157.27, 140.50, 139.89, 136.39, 130.82, 126.71, 125.98, 117.85, 72.77, 72.27, 56.90, 54.43, 34.95, 34.04, 33.85, 33.36, 33.13, 31.43, 31.37, 29.43, 25.86, 24.33, 24.28; IR (KBr): 2952, 2935, 2861, 1629, 1468, 1441, 1362, 1272 cm^{-1}; HRMS (ESI): m/z Calcd. for $C_{38}H_{58}N_3O_2$ [M + H]$^+$: 588.4529, found: 588.4520.

L7. Yield: 73%. mp 66–69 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.69 (s, 1H), 13.48 (s, 1H), 8.33 (s, 1H), 8.29 (s, 1H), 7.36 (d, J = 1.6 Hz, 1H), 7.33 (d, J = 2.0 Hz, 1H), 7.07 (d, J = 2.0 Hz, 1H), 7.00 (d, J = 2.0 Hz, 1H), 3.72–3.75 (m, 4H), 3.53–3.61 (m, 2H), 3.28–3.37 (m, 2H), 2.51–2.54 (m, 4H), 1.48–1.95 (m, 8H), 1.43 (s, 9H), 1.26 (s, 9H), 1.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.72, 165.18, 158.01, 157.38, 140.52, 139.92, 136.42, 130.86, 126.96, 126.76, 126.01, 125.79, 124.02, 117.87, 72.85, 72.26, 67.05, 66.82, 56.75, 53.77, 53.16, 34.98, 34.07, 33.85, 33.44, 33.14, 31.54, 31.46, 31.39, 31.34, 29.44, 24.36, 24.29; IR (KBr): 2957, 2861, 2800, 1629, 1471, 1441, 1362, 1273, 1118 cm^{-1}; HRMS (ESI): m/z Calcd. for $C_{37}H_{56}N_3O_3$ [M + H]$^+$: 590.4322, found: 590.4319.

L8. Yield: 66%. mp 85–89 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.65 (s, 2H), 8.32 (s, 1H), 8,28 (s, 1H), 7.59 (s, 1H), 7.32 (d, J = 2.4 Hz, 1H), 7.11 (d, J = 2.4 Hz, 1H), 7.02 (s, 1H), 6.99–7.01 (m, 2H), 6.96 (s, 1H), 5.14 (d, J = 16 Hz, 1H), 5.03 (d, J = 16 Hz, 1H), 3.28–3.38 (m, 2H), 1.88–1.95 (m, 4H), 1.68–1.79 (m, 2H), 1.45–1.52 (m, 2H), 1.40 (s, 9H), 1.25 (s, 9H), 1.18 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.93, 165.09, 158.11, 157.13, 141.32, 140.18, 137.84, 136.61, 129.42, 129.07, 128.33, 127.02, 126.14, 123.53, 119.54, 118.12, 117.97, 72.87, 72.29, 45.79, 35.12, 34.23, 34.02, 33.58, 33.14, 31.60, 31.41, 29.56, 24.46, 24.38; IR (KBr): 2967, 2868, 1630, 1509, 1477, 1442, 1363, 1275, 1091, 1050, 881 cm^{-1}; HRMS (ESI): m/z Calcd. for $C_{36}H_{51}N_4O_2$ [M + H]$^+$: 571.4012, found: 571.4009.

L9. Yield: 79%. mp 140–142 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.72 (s, 1H), 13.57 (s, 1H), 8.36 (s, 1H), 8.30 (s, 1H), 7.51 (s, 1H), 7.35 (s, 1H), 7.12 (s, 1H), 7.04 (s, 1H), 4.50–4.63 (m, 2H), 3.52–3.58 (m, 1H), 3.31–3.38 (m, 9H), 1.46–1.97 (m, 12H), 1.41 (s, 9H), 1.26 (s, 9H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.18, 165.01, 162.68, 157.95, 151.36, 140.19, 139.69, 136.60, 133.90, 128.80, 127.05, 125.94, 123.23, 117.73, 116.46, 71.49, 70.09, 50.06, 47.98, 47.39, 45.67, 38.45, 34.97, 34.08, 33.84, 33.65, 32.11, 31.44, 31.20, 29.38, 24.19, 24.12, 21.28, 20.94; IR (KBr): 2954, 2864, 1629, 1600, 1541, 1476, 1442, 1362, 1320, 1274 cm^{-1}; HRMS (ESI): m/z Calcd. for $C_{40}H_{60}N_5O_2$ [M + H]$^+$: 642.4747, found: 642.4753.

Synthesis of ligand L3. A mixture of 1,2-diaminocyclohexane (0.083 g, 72.8 mmol) and compound **13** (0.60 g, 1.5 mmol) in ethanol (60 mL) was stirred for 2 h at room temperature before it was allowed to remove the solvent. The crude product was further purified by column chromatography on silica gel using dichloromethane/methanol (10 : 1) as mobile phase to give **L3** as yellow solid (0.59 g, 95%). mp 107–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.48 (s, 2H), 8.21 (s, 2H), 7.68–7.77 (m, 8H), 7.41–7.45 (m, 2H), 7.33–7.39 (m, 4H), 7.23–7.31 (m, 6H), 7.21 (s, 2H), 6.98 (s, 2H), 3.78–3.85 (m, 2H), 3.64–3.71 (m, 2H), 3.26–3.28 (m, 2H), 1.84–1.87 (m, 4H), 1.62–1.65 (m, 2H), 1.42–1.47 (m, 2H), 1.08 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.76, 156.88 (d, J = 5.0 Hz), 140.69 (d, J = 2.5 Hz), 133.56, 133.10, 132.58, 132.12, 131.50 (d, J = 2.2 Hz), 131.17 (d, J = 3.4 Hz), 131.08 (d, J = 3.5 Hz), 128.30 (d, J = 3.2 Hz), 128.18 (d, J = 3.2 Hz), 126.69, 118.69 (d, J = 7.4 Hz), 117.55, 72.38, 33.75, 33.32, 31.20, 30.44, 29.75, 24.17; ^{31}P NMR (161 MHz, $CDCl_3$): δ 30.84; IR (KBr): 3055, 2952, 2860, 1629, 1475, 1437, 1395, 1279, 1195, 1120, 735, 720, 695 cm^{-1}; HRMS (ESI): m/z Calcd. for $C_{54}H_{61}N_2O_4P_2$ [M + H]$^+$: 863.4107, found: 863.4100.

Synthesis of ligand L10. To a solution of **L5** (0.58 g, 1.0 mmol) in acetonitrile (20 mL) in a 50 mL flask wrapped in aluminium foil was added iodomethane (0.10 mL, 1.5 mmol). The mixture was stirred for 24 h at room temperature before removing the solvent. The residue was purified by column chromatography on silica gel using dichloromethane/methanol (10 : 1) as mobile phase to give **L10** as yellow solid (0.50 g, 70%). mp 146–148 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 14.31 (s, 1H), 13.60 (s, 1H), 8.36 (s, 1H), 8.30 (s, 1H), 7.82 (d, J = 2.4 Hz, 1H), 7.34 (d, J = 2.4 Hz, 1H), 7.28 (d, J = 2.4 Hz, 1H), 7.00 (d, J = 2.4 Hz, 1H), 4.78 (d, J = 12 Hz, 1H), 4.66 (d, J = 12 Hz, 1H), 3.72 (m, 1H), 3.56–3.69 (m, 1H), 3.42–3.53 (m, 3H), 3.28–3.34 (m, 1H), 3.12 (s, 3H), 1.91–2.04 (m, 4H), 1.49– 1.80 (m, 4H), 1.43 (t, J = 4.0 Hz, 6H), 1.40 (s, 9H), 1.26 (d, J = 4.0 Hz, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.75, 164.75, 160.08, 157.97, 141.59, 140.16, 136.64, 135.87, 131.13, 126.99, 125.80, 118.18, 117.78, 114.42, 72.26, 71.41, 59.54, 56.10, 47.09, 34.99, 34.15, 34.10, 33.49, 32.56, 31.46, 31.36, 29.45, 29.36, 24.28, 24.16, 8.75; IR (KBr): 2954, 2862, 1630, 1535, 1476, 1441, 1391, 1362, 1273 cm^{-1}; HRMS (ESI): m/z Calcd. for $C_{38}H_{60}N_3O_2$ [M – I]$^+$: 590.4686, found: 590.4690.

General procedure of cyanosilylation of aldehydes. [Caution! TMSCN is toxic and volatile and must be used in well ventilated hood] To a solution of ligand **L5** (1.3 mg, 2.2 × 10^{-3} mmol)

in 2.5 mL CH_2Cl_2 in a flame-dried reaction vessel, was added $Ti(O^iPr)_4$ (0.6 μL, 2.0×10^{-3} mmol) in glove box. After stirring the mixture at ambient temperature for 2 h, aldehyde (4 mmol) and TMSCN (8 mmol) were added. The reaction was stirred for the time shown in Table 2 at room temperature. Then 2 N HCl (40 mL) and ethyl acetate (20 mL) was added to quench the reaction. The resulting mixture was stirred for 5 h and then extracted with ethyl acetate (3×15 mL). The organic layer was washed with brine and dried over anhydrous Na_2SO_4. The crude product was further purified by column chromatography (petrol ether/ethyl acetate = 10 : 1) to give the cyanohydrins.

2-Hydroxy-2-phenylacetonitrile. Colourless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.50 (m, 2H), 7.41–7.44 (m, 3H), 5.49 (d, J = 6.0 Hz, 1H), 3.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 135.24, 129.93, 129.30, 126.80, 119.07, 63.56; IR (neat): 3416, 2249; HRMS (ESI): m/z Calcd. for $C_{10}H_{10}NO_3$ [M + CH_3COO]$^-$: 192.0611, found: 192.0609.

2-Hydroxy-2-*p*-tolylacetonitrile. Colourless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.4 Hz, 1H), 5.48 (s, 1H), 2.88 (s, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 139.93, 132.34, 129.83, 126.70, 119.07, 63.36, 21.24; IR (film): 3416, 2249; HRMS (ESI): m/z Calcd. for $C_{11}H_{12}NO_3$ [M + CH_3COO]$^-$: 206.0817, found: 206.0814.

2-Hydroxy-2-(4-methoxyphenyl)acetonitrile. White solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 8.8 Hz, 2H), 6.96 (d, J = 8.8 Hz, 2H), 5.48 (s, 1H), 3.85 (s, 3H), 3.21 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 160.67, 128.43, 127.64, 119.25, 114.61, 63.20, 55.54; IR (film): 3418, 2247; HRMS (ESI): m/z Calcd. for $C_{11}H_{12}NO_4$ [M + CH_3COO]$^-$: 222.0766, found: 222.0765.

2-Hydroxy-2-(2-methoxyphenyl)acetonitrile. Colourless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.43 (m, 2H), 6.97–7.04 (m, 2H), 5.56 (d, J = 8.8 Hz, 1H), 3.55 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 156.83, 131.27, 128.17, 123.76, 121.22, 118.81, 111.26, 60.72, 55.80; IR (film): 3417, 2248; HRMS (ESI): m/z Calcd. for $C_{11}H_{12}NO_4$ [M + CH_3COO]$^-$: 222.0766, found: 222.0762.

2-Hydroxy-2-(4-nitrophenyl)acetonitrile. Slightly yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (d, J = 8.4 Hz, 2H), 7.89 (d, J = 8.4 Hz, 2H), 6.45 (s, 1H), 6.05 (s, 1H); ^{13}C NMR (100 MHz, acetone-d_6): 148.89, 144.37, 128.10, 124.44, 119.52, 62.30; IR (film): 3406, 2250; HRMS (ESI): m/z Calcd. for $C_8H_5N_2O_3$ [M – H]$^-$: 177.0300, found: 177.0301.

2-(4-Chlorophenyl)-2-hydroxyacetonitrile. Slightly yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.48 (m, 4H), 5.53 (s, 1H), 3.13 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 135.87, 133.57, 129.39, 128.02, 118.69, 62.77; IR (KBr): 3403, 2252; HRMS (ESI): m/z Calcd. for $C_{10}H_9NO_3Cl$ [M + CH_3COO]$^-$: 226.0271, found: 226.0274.

(*E*)-2-Hydroxy-4-phenylbut-3-enenitrile. Slightly yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.43 (m, 5H), 6.93 (d, J = 16.0 Hz, 1H), 6.26 (dd, J = 6.0, 15.8 Hz, 1H), 5.17 (d, J = 5.6 Hz, 1H), 2.66 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 135.28, 134.78, 129.10, 128.86, 127.12, 122.22, 118.40, 61.82; IR (film): 3406, 2245; HRMS (ESI): m/z Calcd. for $C_{12}H_{12}NO_3$ [M + CH_3COO]$^-$: 218.0817, found: 218.0819.

2-(Furan-2-yl)-2-hydroxyacetonitrile. Colourless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, J = 1.2 Hz, 1H), 6.60 (d, J = 3.2 Hz, 1H), 6.42–6.43 (m, 1H), 5.55 (s, 1H), 3.24 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 147.62, 144.34, 117.03, 110.93, 110.14, 56.94; IR (neat): 3396, 2254; HRMS (ESI): m/z Calcd. for $C_8H_8NO_4$ [M + CH_3COO]$^-$: 182.0453, found: 182.0455.

2-Hydroxynonanenitrile. Colourless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.45-4.50 (m, 1H), 2.74 (s, 1H), 1.82–1.87 (m, 2H), 1.46–1.52 (m, 2H), 1.28–1.33 (m, 8H), 0.87–0.90 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 120.17, 61.24, 35.10, 31.64, 28.99, 28.87, 24.55, 22.57, 14.03; IR (neat): 3442, 2248; HRMS (ESI): m/z Calcd. for $C_{11}H_{20}NO_3$ [M + CH_3COO]$^-$: 214.1443, found: 214.1441.

2-Hydroxy-3-methylbutanenitrile. Colourless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.28 (d, J = 6.0 Hz, 1H), 3.06 (s, 1H), 2.00–2.10 (m, 1H), 1.06–1.11 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 119.46, 67.06, 33.14, 17.81, 17.35; IR (neat): 3442, 2247; HRMS (ESI): m/z Calcd. for $C_7H_{12}NO_3$ [M + CH_3COO]$^-$: 158.0817, found: 158.0819.

Conclusions

In summary, we have developed a series of new salen ligands bearing an appended Lewis base on the 3-position of one aromatic ring and succeeded in applying them to the cyanosilylation of various aldehydes with TMSCN by combining with $Ti(O^iPr)_4$ as a bifunctional catalyst. The catalyst system with regard to ligand **L5** bearing a diethylamino group proved to be more active even at a high [aldehyde]/[catalyst] ratio up to 50000 under mild conditions. Although the detailed mechanism is not clear, kinetic experiments suggest that an intramolecule cooperative catalysis exists in the cyanosilylation using the unsymmetric salen ligands in conjunction with $Ti(O^iPr)_4$ as catalyst. It is tentatively proposed wherein the central metal ion Ti(IV) is suggested to play a role of Lewis acid to activate aldehydes while the appended Lewis base to activate TMSCN.

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Notes and references

1 (*a*) W. R. Jackson, H. A. Jacobs, B. R. Matthews, G. S. Jayatilake and K. G. Watson, *Tetrahedron Lett.*, 1990, **31**, 1447; (*b*) F. Effenberger and U. Stelzer, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 873; (*c*) M. North, *Synlett*, 1993, 807; (*d*) F. Effenberger, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 1555; (*e*) R. J. H. Geregory, *Chem. Rev.*, 1999, **99**, 3649; (*f*) J. M. Brunel and I. P. Holmes, *Angew. Chem., Int. Ed.*, 2004, **43**, 2752; (*g*) M. North, *Tetrahedron: Asymmetry*, 2003, **14**, 147.

2 (*a*) K. D. Surya and A. G. Richard, *J. Mol. Catal. A: Chem.*, 2005, **232**, 123; (*b*) P. Saravanan, R. V. Anand and V. R. Singh, *Tetrahedron Lett.*, 1998, **39**, 3823; (*c*) M. North, D. L. Usanov and C. Young, *Chem. Rev.*, 2008, **108**, 5146.

3 (*a*) S. K. Tian, R. Hong and L. Deng, *J. Am. Chem. Soc.*, 2003, **125**, 9900; (*b*) S. E. Denmark and W. Chung, *J. Org. Chem.*, 2006, **71**, 4002.

4 (*a*) Y. Fukuda, Y. Maeda, S. Ishii, K. Kondo and T. Aoyama, *Synthesis*, 2006, **4**, 589; (*b*) J. J. Song, F. Gallou, J. T. Reeves, Z. Tan, N. K. Yee

and C. H. Senanayake, *J. Org. Chem.*, 2006, **71**, 1273; (*c*) Y. Suzuki, A. Bakar, M. D. Kazuyuki Muramastsu and M. Sato, *Tetrahedron*, 2006, **62**, 4227.
5 (*a*) Y. N. Belokon, S. Caveda-Cepas, B. Green and M. North, *J. Am. Chem. Soc.*, 1999, **121**, 3968; (*b*) S. S. Kim and D. H. Song, *Eur. J. Org. Chem.*, 2005, 1777; (*c*) C. Baleizao, B. Gigante, H. Garcia and A. Corma, *Tetrahedron Lett.*, 2003, **44**, 6813; (*d*) N. Kurono, K. Arai, M. Uemura and T. Ohkuma, *Angew. Chem., Int. Ed.*, 2008, **47**, 6643.
6 (*a*) P. G. Gassman and J. L. Talley, *Tetrahedron Lett.*, 1978, **19**, 3773; (*b*) N. Kurono, M. Yamaguchi, K. Suzuki and T. Ohkuma, *J. Org. Chem.*, 2005, **70**, 6530.
7 (*a*) Y. Hamashima, D. Sawada, H. Nogami, M. Kanai and M. Shibasaki, *Tetrahedron*, 2001, **57**, 805; (*b*) M. Kanai, N. Kato, E. Ichikawa and M. Shibasaki, *Synlett*, 2005, **10**, 1491; (*c*) N. H. Khan, R. I. Kureshy, S. H. R. Abdi, S. Agrawal and R. V. Jasra, *Coord. Chem. Rev.*, 2008, **252**, 593; (*d*) W. T. Wang, X. H. Liu, L. L. Lin and X. M. Feng, *Eur. J. Org. Chem.*, 2010, 4751.
8 (*a*) Y. Hamashima, D. Sawada, M. Kanai and M. Shibasaki, *J. Am. Chem. Soc.*, 1999, **121**, 2641; (*b*) M. Shibasaki, M. Kanai and K. Funabashi, *Chem. Commun.*, 2002, 1989; (*c*) M. Kanai, Y. Hamashima and M. Shibasaki, *Tetrahedron Lett.*, 2000, **41**, 2405; (*d*) M. Shibasaki, M. Kanai and K. Funabashi, *J. Am. Chem. Soc.*, 2000, **122**, 7412.
9 J. Casas, C. Nájera, J. M. Sansano and J. M. SaáBinolam, *Org. Lett.*, 2002, **4**, 2589.
10 Y. C. Qin, L. Liu and L. Pu, *Org. Lett.*, 2005, **7**, 2381.
11 Y. B. Kim, M. K. Kim, S. H. Kang and Y. H. Kim, *Synlett*, 2005, 1995.
12 B. M. Trost and S. M. Sánchez, *Synlett*, 2005, **4**, 627.
13 (*a*) B.-Q. Zeng, X. Zhou, X.-H. Liu and X.-M. Feng, *Tetrahedron*, 2007, **63**, 5129; (*b*) W.-T. Wang, X.-H. Liu, L.-L. Lin and X.-M. Feng, *Eur. J. Org. Chem.*, 2010, 4751.
14 (*a*) Z.-H. Yang, Z.-H. Zhou, K. He, L.-X. Wang, G.-F. Zhao and C.-C Tang, *Tetrahedron: Asymmetry*, 2003, **14**, 3937; (*b*) J. M. Brunel, O. Legrand and G. Buono, *Tetrahedron: Asymmetry*, 1999, **10**, 1979; (*c*) K. He, Z. Zhou, L. Wang, K. Li, G. Zhou and C. Tang, *Tetrahedron*, 2004, **60**, 10505.
15 F. Yang, S.-P. Wei and J.-S. You, *Chem.–Eur. J.*, 2008, **14**, 2223.
16 (*a*) Z.-B. Zeng, G.-F. Zhao, P. Gao, H.-Y. Tang, B. Chen, Z.-H. Zhou and C.-C. Tang, *Catal. Commun.*, 2007, **8**, 1443; (*b*) Y.-Z. Jiang, L.-Z. Gong, X.-M. Feng, W.-H. Hu, W.-D. Pan, Z. Li and A.-Q. Mi, *Tetrahedron*, 1997, **53**, 14327; (*c*) S. Liang and X.-R. Bu, *J. Org. Chem.*, 2002, **67**, 2702; (*d*) Z.-H. Yang, Z.-H. Zhou and C.-C. Tang, *Synth. Commun.*, 2001, **31**, 3031; (*e*) Z.-P. Zhang, Z. Wang, R.-Z. Zhang and K.-L. Ding, *Angew. Chem., Int. Ed.*, 2010, **49**, 6746.
17 (*a*) W.-M. Ren, Z.-W. Liu, Y.-Q. Wen, R. Zhang and X.-B. Lu, *J. Am. Chem. Soc.*, 2009, **131**, 11509; (*b*) W.-M. Ren, X. Zhang, Y. Liu, J.-F. Li, H. Wang and X.-B. Lu, *Macromolecules*, 2010, **43**, 1396; (*c*) X. Zhang, Y.-B. Jia, X.-B. Lu, B. Li, H. Wang and L.-C. Sun, *Tetrahedron Lett.*, 2008, **49**, 6589.
18 (*a*) E. J. Campbell and S. T. Nguyen, *Tetrahedron Lett.*, 2001, **42**, 1221; (*b*) M. Holbach, X.-L. Zheng, C. Burd, C. W. Jones and M. Weck, *J. Org. Chem.*, 2006, **71**, 2903.
19 (*a*) P. Steenwinkela, S. Kolmschota, R. A. Gossagea, P. Dania, N. Veldmanb, A. L. Spekb and G. van Koten, *Eur. J. Inorg. Chem.*, 1998, 477; (*b*) E. Lindner, M. Khanfar and M. Steimann, *Eur. J. Inorg. Chem.*, 2001, 2411.
20 (*a*) S. Copinga, P. G. Tepper, C. J. Grl, A. S. Horn and M. L. Dubocovich, *J. Med. Chem.*, 1993, **36**, 2891; (*b*) A. Furstner, M. M. Domostoj and B. Scheiper, *J. Am. Chem. Soc.*, 2006, **128**, 8087(supportiong information).
21 (*a*) M. W. Fennie, E. F. DiMauro, E. M. O'Brien, V. Annamalai and M. C. Kozlowski, *Tetrahedron*, 2005, **61**, 6249; (*b*) E. F. DiMauro and M. C. Kozlowski, *Org. Lett.*, 2001, **3**, 3053.

